Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

Maine Department of Health and Human Services
Office of MaineCare Services - Pharmacy Unit
11 State House Station
Augusta, Maine 04333-0011
Toll Free: (866) 796-2463; TTY: Dial 711 (Maine Relay)
Fax: (207) 287-8601

TO: Maine Drug Utilization Review Board
DATE: 12/15/22
RE: Maine DUR Board Meeting minutes from December 13, 2022

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Linda Glass, MD			X
Kathleen Polonchek, MD			X
Erin Ackley, PharmD.	X		
Charmaine Patel, MD	X		
Caitlin Morrow, PharmD.	X		
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Jeff Barkin, MD, Change Healthcare	X		
Anne-Marie Toderico, PharmD MaineCare Pharmacy Director	X		

Guests of the Board:

CALL TO ORDER: 6:30PM

Erin Ackley called the meeting to order at 6:30 PM.

PUBLIC COMMENTS

Dr. John Flatt from Marinus Pharm: Highlighted the attributes of Ztalmy.

Sylvia Poulos from Recordati Rare Diseases: Highlighted the attributes of Carbaglu.

OLD BUSINESS

DUR MINUTES

Approval of November 1, 2022, DUR meeting minutes

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE- ANNE-MARIE TODERICO

No updated at this time.

ADDINTIONAL OFFERS

- Hyperammonia Treatments- Carglumic Acid
- Hyperammonia Treatments-Carbaglu
- Pulmonary Anti-Hypertensives- Tadliq
- Urea Cycle Disorder Agents-Pheburane

Recommendation: Add Carglumic Acid to preferred. Add Carbaglu, Tadliq and Phenburane to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

BIOSIMILAR

- Cimerli (ranibizumab- eqrn)- biosimilar, and interchangeable with Lucentis
- Fylnetra (pegfilgrastim-pbbk)- biosimilar to Neulasta

Recommendation: Add Cimerli and Fylnetra to non-preferred on the PDL.

Board Decision: The Board unanimously approved the above recommendation.

NEW BUSINESS

2023 RETRODUR INITIATIVES CALENDAR

December 13, 2022

- Data presentation: Appropriate use of asthma controller medications
- Introduce: Blood glucose test strips in CGM users

March 14, 2023:

- Data presentation: blood glucose test strips in CGM users
- Introduce: Effect of trikafta on the cost and quality of care of patients with cystic fibrosis

June 13, 2023:

- Data presentation: Effect of trikafta on the cost and quality of care of patients with cystic fibrosis
- Introduce: Antianxiety/sedatives in children

September 12, 2023:

- Data presentation: Antianxiety/sedatives in children
- Introduce: Triple therapy: opioids, benzodiazepines, and skeletal muscle relaxants

November 7, 2023:

- Data presentation: 2024 Potential RetroDUR Initiatives

December 12, 2023:

- Data presentation: Triple therapy: opioids, benzodiazepines, and skeletal muscle relaxants
- Introduce: Hemlibra on cost and quality of care of hemophilia a patients

2024 Meeting #1:

- Data presentation: Hemlibra on cost and quality of care of hemophilia a patients

Board Decision: None at this time.

PRESENTATION: APPROPRIATE USE OF ASTHMA CONTROLLER MEDICATIONS

The National Heart, Lung and Blood Institute has published Guidelines for the Diagnosis and Management of Asthma.The treatment of asthma is done in a step-wise manner, and depending on disease severity, a combination of several agents may be needed. For anyone who requires use of a

short acting agent > 2 days/week, a controller medication daily is recommended. The Guidelines state that the frequency of short acting beta-adrenergic inhaler (SABA) use can be clinically useful as a measure of disease activity since increased use of a SABA has been associated with increased risk for death or near death in patients who have asthma. Use of more than one SABA canister every one to two months is also associated with an increased risk of an acute exacerbation. Therefore, the use of more than one SABA canister (e.g., albuterol 200 puffs per canister) during a one-month period most likely indicates over reliance on this drug and suggests inadequate control of asthma. Updated GINA guidelines state that all adults and adolescents on a SABA, even those with mild asthma, should be on an ICS controller treatment. Inhaled corticosteroids (ICS) are the preferred long-term control therapy in asthma for all ages, although leukotriene receptor antagonists (LTRA) are listed as an alternative. Long-acting beta-adrenergic inhalers (LABAs) should never be used without first using ICS inhalers due to the increased risk of asthma exacerbations and death. Change Healthcare used paid, non-reversed pharmacy claims with dates of service from 1/1/2022 through 12/09/2022 excluding members with Part D, MaineRX and TPL. Change Healthcare reviewed Maine paid non-reversed pharmacy claims with dates of service from 1/1/2022 through 12/09/2022 and identified the members with the diagnosis of asthma and excluded members with diagnoses of cystic fibrosis, COPD or emphysema. Members were stratified by age and the number of short acting inhalers used per year. Additionally, we identified how many members who were prescribed a SABA were also prescribed a controller medication, either an ICS inhaler or an ICS combination inhaler. The prescribers for these members were identified to look at providers who are possibly practicing outside of guideline recommendations, perhaps identifying those who would be appropriate for more targeted education. From the data above, it is hard to draw conclusions about whether the controller medications are being used appropriately. For the members prescribed less than 1 cannister of SABA a month, the addition of controller medications did not seem to impact either ED visits or hospital admissions. This could be because the member was non-compliant with the controller medications, especially if their asthma symptoms were episodic. Additionally, it is likely that young children are not proficient in using inhalers, especially if not used daily. Forgetting to use controller medication is likely more of an issue for members whose symptoms are intermittent. For the members prescribed higher number of cannisters a month, the numbers were too small to draw any conclusions. It may be that they are more consistent with inhaler use, which prevents need for ED or hospital care. The data here support the notion that patient education is a necessary part of disease management. Members need to understand the importance of recognizing early symptoms, correct use of inhalers, consistent use of controller medications and, in most instances, reliance of SABAs alone. There were no prescriber patterns that warrant targeted education.

Recommendation: The likely best approach to improve compliance is a general communication to primary care providers about the importance of asthma education and management. Potential resources:
https://ginasthma.org/pocket-guide-for-asthma-management-and-prevention/
https://www.nhlbi.nih.gov/sites/default/files/publications/AsthmaCliniciansGuideDesign-508.pdf
MICIS: Education Topics (micismaine.org)

Board Decision: The Board unanimously approved the above recommendation. Caitlin asked if the data could be looked at regionally as so many specialty offices are closed or not accepting new patients more and more primary cares are having to treat those patients unable to get in with a specialist.

INDTRODUCE: GLUCOSE TEST STRIP USAGE WITH CGMS

The use of continuous glucose monitors (CGMs) has become accepted standard of care for both type 1 diabetes and insulin dependent type 2 diabetes mellitus. While the value of CGM in type 2 diabetics not requiring insulin is uncertain due to rare occurrence of hypoglycemia, there are studies that show improvement in A1c levels compared with conventional blood glucose monitoring. In addition, blood glucose monitoring with fingersticks has potential errors due to poor compliance, dirty or contaminated meters, improper storage of test strips, expired test strips and poor skin preparation. Use of CGMs has improved glycemic control and over time, as technology has improved, there is less need to rely on testing to verify the CGM results. Initially when CGMs came on the market, conventional testing with finger sticks was recommended multiple times a day. As CGMs have evolved, however, the recommendation now is to corroborate results when the CGM reading seems inaccurate, either due to symptoms or unexplained fluctuations in the readings. Blood glucose monitoring is still required during CGM warm-up periods, to double check high and low values and sometimes for calibrating CGMs. For members using CGMs, it is expected that the increased expense of the monitors, sensors and supplies would be somewhat offset by decreased need to do fingerstick testing, and therefore decreased cost of glucose test strips.

Recommendation: We will use paid, non-reversed Medicaid pharmacy claims from 1calendar year 2021, excluding members with Part D, MaineRX and TPL. We will look at all pharmacy claims for members who began Dexcom G6 or Freestyle Libre CGM, we will evaluate blood glucose test strip usage in the 1-year time frame prior to the CGM period and for 1 year after the CGM period.

Board Decision: None needed.

NEW DRUG REVIEW

Auvelity® (dextromethprphan- bupropion); **PDL category-** Antidepressants- Selected SSRI and Others

Auvelity® is a combination of dextromethorphan hydrobromide (an uncompetitive NMDA receptor antagonist and sigma 1 receptor agonist) and bupropion HCl (an aminoketone and CYP450 2D6 inhibitor). The mechanism of dextromethorphan in the treatment of MDD is unclear. The mechanism of action of bupropion in the treatment of MDD is unclear; however, it may be related to noradrenergic and/or dopaminergic mechanisms. Bupropion increases plasma levels of dextromethorphan by competitively inhibiting CYP2D6, which catalyzes a major biotransformation pathway for dextromethorphan. Bupropion is a relatively weak inhibitor of the neuronal reuptake of norepinephrine and dopamine and does not inhibit monoamine oxidase or the reuptake of serotonin. It is indicated for the treatment of major depressive disorder (MDD) in adults. The safety and efficacy of Auvelity® for the treatment of MDD in adults were assessed in a placebo-controlled clinical study (Study 1) and confirmatory evidence included a second study comparing Auvelity® to bupropion HCl SR tablets (Study 2). In a 6-week, placebo-controlled study that compared Auvelity® with placebo, Auvelity® was statistically significantly superior to placebo in improvement of depressive symptoms as measured by decrease in MADRS total score at week 6. Per the manufacturer's website, "it's the first and only rapid-acting oral antidepressant labeled to start working at 1 week." In study 1, the difference between Auvelity® and placebo in change from baseline in MADRS total score was statistically significant at week 1 and at week 2. In addition, in a second study comparing Auvelity® with bupropion SR tablets, the results of the study demonstrated that dextromethorphan contributes to the antidepressant properties of Auvelity®. There is no evidence at this time to support that Auvelity® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Auvelity® to non-preferred.

Clinical Criteria:

- Use of individual ingredients or other preferred medications.

Enjaymo® (sutimlimab-jome); **PDL category-** CAD

Sutimlimab-jome, the active ingredient of Enjaymo®, is a classical complement inhibitor. Sutimlimab-jome is an immunoglobulin G (IgG), subclass 4 (IgG4) monoclonal antibody (mAb) that inhibits the classical complement pathway (CP) and specifically binds to complement protein component 1, s subcomponent (C1s), a serine protease which cleaves C4. Sutimlimab-jome does not inhibit the lectin and alternative pathways. Inhibition of the classical complement pathway at the level of C1s prevents deposition of complement opsonins on the surface of red blood cells (RBCs), resulting in inhibition of hemolysis in patients with CAD. It is indicated to decrease the need for red blood cell transfusion due to hemolysis in adults with cold agglutinin disease (CAD). The safety and efficacy of Enjaymo® were assessed in an open-label, single-arm, 6-month trial (N=24; CARDINAL study). After the completion of the 6-month treatment period, patients continued to receive Enjaymo® in a long-term safety and durability of response extension phase for an additional 24 months. Efficacy was based on responder rate, which was defined as a patient with an increase from baseline in Hgb level ≥2g/dL or a Hgb level ≥12g/dL at the treatment assessment time point, no blood transfusion from week 5 through week 26, and no treatment for CAD beyond what was permitted per protocol from week 5 through week 26. The responder rate with Enjaymo® use was 54%. There is no evidence at this time to support that Enjaymo® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Enjaymo® to non-preferred.

Clinical Criteria:

- Indicated to decrease the need for red blood cell transfusion due to hemolysis in adults with cold agglutinin disease (CAD).

Entadfi® (finasteride & tadalafil); **PDL category**- BPH

Entadfi® is combination of finasteride (a specific inhibitor of steroid Type II 5α-reductase, an intracellular enzyme that converts the androgen testosterone into 5α-dihydrotestosterone or DHT) and tadalafil (a selective inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 or PDE5). Type II 5α-reductase metabolizes testosterone to DHT in the prostate gland, liver, and skin. DHT induces androgenic effects by binding to androgen receptors in the cell nuclei of these organs. Finasteride is a competitive and specific inhibitor of Type II 5α-reductase with which it slowly forms a stable enzyme complex. In humans, the 5α reduced steroid metabolites in blood and urine are decreased after administration of finasteride. The mechanism for reducing BPH symptoms with tadalafil has not been established. PDE5 is found in the smooth muscle of the corpus cavernosum, prostate, and bladder, among others. It is indicated to initiate treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) in men with an enlarged prostate for up to 26 weeks. Note that Entadfi® is not recommended for more than 26 weeks because the incremental benefit of tadalafil decreases from 4 weeks until 26 weeks, and the incremental benefit beyond 26 weeks is not known. The efficacy of Entadfi® is based on an adequate and well-controlled study of tadalafil co-administered with finasteride. A double-blind, parallel-design study of 26 weeks in duration randomized men (N=696) to start either tadalafil 5mg with finasteride 5mg or placebo

with finasteride 5mg in treating signs and symptoms of BPH in men with an enlarged prostate (>30 cc). Results suggested that tadalafil and finasteride administered together demonstrated statistically significant improvement in the signs and symptoms of BPH compared to placebo with finasteride, as measured by the total symptoms score (IPSS) at 12 weeks. However, the magnitude of the treatment difference between placebo/finasteride and tadalafil/finasteride decreased from 1.7 points at week 4 to 1.0 point at week 26. The incremental benefit of Entadfi® beyond 26 weeks is unknown.

Recommendation: Entadfi® to non-preferred.

Clinical Criteria:

- Use of individual ingredients preferred (Finasteride and tadalafil).
- Entadfi® is not recommended for more than 26 weeks

Hyftor® (sirolimus) **PDL category-** Topical, Immunosuppressants

Sirolimus, the active ingredient of Hyftor®, is an mTOR (mammalian target of rapamycin) inhibitor immunosuppressant for topical use. The mechanism of action for its approved indication is not known. Tuberous sclerosis is associated with genetic defects in TSC1 and TSC2 which leads to the constitutive activation of mTOR. Sirolimus inhibitors mTOR activation. It is indicated for the treatment of facial angiofibroma associated with tuberous sclerosis in adults and pediatric patients 6 years of age and older. The safety and efficacy of Hyftor® were assessed in a single, randomized, double-blind, vehicle-controlled, multicenter, phase 3 trial that was conducted in Japan and included adults and pediatric patients 6 years of age and older with facial angiofibroma associated with tuberous sclerosis. A greater number in the Hyftor®-treated group were assessed by the investigator as 'improved' or 'markedly' improved as compared with the vehicle-treated group. One noted reference source suggests that laser therapy and dermabrasion may improve skin lesions associated with tuberous sclerosis complex. Topical mTOR inhibitors, including sirolimus, are listed as "possibly" improving lesions.

Recommendation: Hyftor® to non-preferred.

Clinical Criteria:

- For the treatment of patients ≥ 6 years of age.
- Clinical PA required for appropriate diagnosis and clinical parameters.

Korsuva® (difelikefalin); **PDL category**- Pruritus associated with CKD

Difelikefalin, the active ingredient of Korsuva®, is a kappa opioid receptor (KOR) agonist. The relevance of KOR activation to therapeutic effectiveness is not known. It is indicated for the treatment of moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD). Korsuva® has not been studied in patients on peritoneal dialysis and is not recommended for use in this population. The safety and efficacy of Korsuva® were assessed in two randomized, multicenter, double-blind, placebo-controlled trial that enrolled subjects 18 years of age and older undergoing HD who had moderate-to-severe pruritus (N=851). In both trials, subjects received IV bolus injections of Korsuva® into the venous line of the hemodialysis circuit at the end of each hemodialysis session or placebo three times per week for 12 weeks. In both trials, a 7-day run-in period prior to randomization was used to confirm that each subject had moderate-to-severe pruritus and to establish a baseline itch intensity, as measured by the patient-reported daily 24-hour Worst Itching Intensity Numerical Rating Scale (WI-NRS) scores (0 'no itch' to 10 'worst itch imaginable'). Its efficacy

was assessed in 2 randomized, double-blind, placebo-controlled trials that included adults undergoing HD who had moderate-to-severe pruritus. In each trial, efficacy was assessed based on the proportion of subjects achieving a 4-point or greater improvement (reduction) from baseline in the weekly mean of the daily 24-hour WI-NRS score at week 12; and results suggested that more in the Korsuva ®group achieved ≥4-point improvement from baseline in WI-NRS score compared with placebo (NNT 6 in Study 1 and NNT 9 in Study 2). There is no evidence at this time to support that Korsuva® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Korsuva® to non-preferred.

Ryaltris® (olopatadine HCL and Mometasone furoate spray); **PDL category**- Antiasthmatic- Nasal Steriods

Dexmedetomidine, the active ingredient of Igalmi®, is an alpha-2 adrenergic receptor agonist. The mechanism of action of Igalmi® for its approved indication is thought to be due to activation of presynaptic alpha-2 adrenergic receptors. It is indicated for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adults. The safety and effectiveness of Igalmi® have not been established beyond 24 hours from the first dose. The safety and efficacy of Igalmi® were assessed in 2 randomized, double-blind, placebo-controlled, fixed-dose studies: Study 1: This study included adults (N=380) who met DSM-5 criteria for schizophrenia, schizoaffective or schizophreniform disorder. The included population was 18 to 71 years of age (mean 46 years), while 37% were female and 20% were white. Study 2: This study included adults (N=378) who met DSM-5 criteria for bipolar I or II disorder. The included population was 18 to 70 years of age (mean 47 years), while 45% were female and 41% were white. The safety and effectiveness of Igalmi® have not been established beyond 24 hours from the first dose. Results suggested that in both studies, the mean change from baseline in the PEC total score at 2 hours after the first dose in patients treated with 180mcg and 120mg of Igalmi® was statistically greater than in patients who received placebo.

Recommendation: Ryaltris® to non-preferred.

Clinical Criteria:

- Use of individual ingredients or other preferred agents.

Sotyktu® (deucravacitinib); **PDL category**- Psoriasis Biologicals

Deucravacitinib, the active ingredient of Sotyktu®, is a tyrosine kinase 2 (TYK2) inhibitor. TYK2 is a member of the Janus kinase (JAK) family. Deucravacitinib binds to the regulatory domain of TYK2, stabilizing an inhibitory interaction between the regulatory and the catalytic domains of the enzyme. This results in allosteric inhibition of receptor-mediated activation of TYK2 and its downstream activation of Signal Transducers and Activators of Transcription (STATs) as shown in cell-based assays. JAK kinases, including TYK2, function as pairs of homo- or heterodimers in the JAK-STAT pathways. TYK2 pairs with JAK1 to mediate multiple cytokine pathways and also pairs with JAK2 to transmit signals as shown in cell-based assays. The precise mechanism linking inhibition of TYK2 enzyme to therapeutic effectiveness for its approved indication is not currently known. It is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. It is not recommended for use in combination with other potent immunosuppressants. he safety and efficacy of Sotyktu® were assessed in 2 multicenter, randomized, double-blind, placebo- and active-controlled trials (PSO-1 and PSO-2) that included adults 18 years of age and older with moderate-to-

severe plaque psoriasis who were eligible for systemic therapy or phototherapy. The authors concluded in both studies that deucravacitinib demonstrated superiority to placebo and apremilast across efficacy endpoints, while being well tolerated.

Recommendation: Sotyktu® to non-preferred.

Spevigo® (spesolimab-sbzo); **PDL category**- Psoriasis Biologicals

Spesolimab-sbzo, the active ingredient of Spevigo®, is an interleukin-36 receptor antagonist. It is a humanized monoclonal IgG1 antibody (mAb) against human IL-36R, produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. It inhibits interleukin-36 (IL-36) signaling by specifically binding to the IL36R. Binding of spesolimab-sbzo to IL36R prevents the subsequent activation of IL36R by cognate ligands (IL-36 α, β, and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways. The precise mechanism linking reduced IL36R activity and treatment of flares of GPP is unclear. It is indicated for the treatment of generalized pustular psoriasis (GPP) flares in adults. The safety and efficacy of Spevigo® were assessed in a randomized, double-blind, placebo-controlled study that included adult subjects with flares of generalized pustular psoriasis (GPP). The authors concluded that further trials are warranted to assess the effect and risks of treatment in patients with pustular psoriasis.

Recommendation: Spevigo® to non-preferred.

Tadliq® (tadalafil); **PDL category**- Pulmonary Antihypertensives

Tadalafil, the active ingredient of Tadliq®, is a selective inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5). Tadalafil is an inhibitor of PDE5, the enzyme responsible for the degradation of cGMP. Pulmonary arterial hypertension is associated with impaired release of nitric oxide by the vascular endothelium and consequent reduction of cGMP concentrations in the pulmonary vascular smooth muscle. PDE5 is the main phosphodiesterase in the pulmonary vasculature. Inhibition of PDE5 by tadalafil increases the concentrations of cGMP resulting in relaxation of pulmonary vascular smooth muscle cells and vasodilation of the pulmonary vascular bed. PDE5 is found in pulmonary vascular smooth muscle, visceral smooth muscle, corpus cavernosum, skeletal muscle, platelets, kidney, lung, cerebellum, and pancreas. It is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominantly patients with NYHA Functional Class II-III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%). There were no new studies found in the Tadliq® prescribing information. The studies in the prescribing information for Tadliq® were those found in the prescribing information of Adcirca®, brand name for tadalafil tablets. Adcirca® has been available for many years, currently has a generic available, and has the same indication as Tadliq®.

Recommendation: Tadliq® to non-preferred.

Clinical Criteria:

- Tadliq approvals will require WHO Group 1 with NYHA Functional Class II-III.

Verkazia® (cyclosporine ophthalmic) **PDL category**- Op- Of Interest

Cyclosporine, the active ingredient of Verkazia®, is a calcineurin inhibitor immunosuppressant agent when administered systemically. Following ocular administration, cyclosporine is thought to act by blocking the release of pro-inflammatory cytokines such as IL-2. The exact mechanism of action for its approved indication is not known. It is indicated for the treatment of vernal keratoconjunctivitis (VKC) in children and adults. The safety and efficacy of Verkazia® for the treatment of VKC were assessed in two randomized, multicenter, double-masked, vehicle-controlled clinical trial (VEKTIS study and NOVATIVE study). In addition, per the manufacturer website, "Verkazia® uses proprietary cationic ophthalmic emulsion technology to increase cyclosporine bioavailability in the cornea." Furthermore, the site indicates that "cationic ophthalmic emulsion enables rapid spread, maximization of contact, prolonged exposure, and near doubling of concentration of cyclosporine in the cornea." Other cyclosporine products are currently available at different doses. There is no evidence at this time to support that Verkazia® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Verkazia® and Cimerli to non-preferred. Cyclosporine Opth 0.05%
Lucentis to preferred.

Vivjoa® (oteseconazole); **PDL category**- Antifungals, Assorted

Oteseconazole, the active ingredient of Vivjoa®, is an antifungal agent. Specifically, it is an azole metalloenzyme inhibitor targeting the fungal sterol, 14α demethylase (CYP51), an enzyme that catalyzes an early step in the biosynthetic pathway of ergosterol, a sterol required for fungal cell membrane formation and integrity. Inhibition of CYP51 results in the accumulation of 14-methylated sterols, some of which are toxic to fungi. Through the inclusion of a tetrazole metal-binding group, oteseconazole has a lower affinity for human CYP enzymes. It is indicated to reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) in females with a history of RVVC who are not of reproductive potential. The safety and efficacy of Vivjoa® were assessed in two multicenter, randomized, double-blind, placebo-controlled trials (Trial 1 and Trial 2) that included adults and post-menarchal pediatric females (N=656) with RVVC (defined as ≥3 episodes of vulvovaginal candidiasis (VVC) in a 12-month period). A total of 219 adults and post-menarchal pediatric females with RVVC were randomized in a third trial, a multicenter, double-blind trial (Trial 3). Although females of reproductive potential were included in the clinical efficacy data, Vivjoa® is contraindicated in females of reproductive potential due to the risk of embryo-fetal toxicity. . There are two recommended Vivjoa® dosage regimens, including a Vivjoa®-only regimen and a fluconazole/Vivjoa® regimen. Vivjoa® is contraindicated in females of reproductive potential as well as in pregnant and lactating women; however, females of reproductive potential were included in the clinical efficacy data. Vivjoa® is the first and only FDA-approved agent for this indication. There is some evidence at this time to suggest that Vivjoa® given over a course of 13 weeks may be more effective than fluconazole given for one week for preventing recurrent acute VVC episodes during the maintenance phase or failure to clear the infection during the induction phase. There is also evidence that it is effective for recurring VVC episodes and results in less of a need to take VVC medication known to treat VVC during the maintenance phase and results in fewer subjects who failed clearing the infection during the induction phase compared to placebo. However, there is no evidence at this time to support that Vivjoa® is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Vivjoa® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

Recommendation: Vivjoa® to non-preferred.

Xenpozyme® (olipudase alfa-rpcp); **PDL category**- ASMD

Olipudase alfa-rpcp, the active ingredient of Xenpozyme®, is a hydrolytic lysosomal sphingomyelin-specific enzyme consisting of 570 amino acids produced in a Chinese hamster ovary cell line by recombinant DNA technology. Acid sphingomyelinase deficiency (ASMD) is a lysosomal storage disease that results from reduced activity of the enzyme acid sphingomyelinase (ASM), caused by pathogenic variants in the sphingomyelin phosphodiesterase 1 gene. ASM degrades sphingomyelin to ceramide and phosphocholine. The deficiency of ASM causes an intra-lysosomal accumulation of sphingomyelin (as well as cholesterol and other cell membrane lipids) in various tissues. Xenpozyme® provides an exogenous source of ASM. Xenpozyme® is not expected to cross the blood-brain barrier or modulate the CNS manifestations of ASMD. It is indicated for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients. The safety and efficacy of Xenpozyme® for the treatment of non-CNS manifestations of ASMD were assessed in 3 clinical trials involving a total of 61 patients with ASMD: Trial 1 in adult patients, Trial 2 in pediatric patients, Trial 3 a long-term trial in pediatric patients. In the adult double-blind, placebo-controlled trial, results suggested that at week 52, an increase of 21% in the mean percent change in % predicted DLco was observed in the Xenpozyme® group as compared to the placebo group. Xenpozyme® treatment resulted in improvements in parameters in the pediatric population as well.

Recommendation: Xenpozyme® to non-preferred.

Clinical Criteria:

- For treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients
- Clinical PA required for appropriate diagnosis and clinical parameters.

Zonisade® (zonisamide); **PDL category**- Anticonvulsants

Zonisamide, the active ingredient of Zonisade®, is chemically classified as a sulfonamide. The exact mechanism of action by which it exerts its anticonvulsant effects is unknown. Zonisamide may produce these effects through action at sodium and calcium channels. In vitro studies suggest that zonisamide blocks sodium channels and reduces voltage-dependent, transient inward currents, consequently stabilizing neuronal membranes. Other in vitro studies have demonstrated that zonisamide suppresses synaptically-driven electrical activity without affecting postsynaptic GABA or glutamate responses or neuronal or glial uptake of [3H]-GABA. Thus, zonisamide does not appear to potentiate the synaptic activity of GABA. It is indicated as an adjunctive therapy for the treatment of partial-onset seizures in adults and pediatric patients 16 years and older. The efficacy of Zonisade® is based upon a bioavailability study comparing Zonisade® oral suspension to zonisamide capsules in healthy subjects. The clinical studies information described in the Zonisade® prescribing information pertains to the zonisamide capsule formulation. Zonisade® offers a different dosage formulation and is the only available ready-to-use liquid formulation of zonisamide.

Zorvye® (roflumilast); **PDL category-** Topical- Antipsoriatics

Roflumilast, the active ingredient of Zoryve®, is a phosphodiesterase 4 (PDE4) inhibitor. Roflumilast and its active metabolite (roflumilast N-oxide) are inhibitors of PDE4. Roflumilast and roflumilast N-oxide inhibition of PDE4 (a major cyclic 3',5'-adenosine monophosphate (cyclic AMP) metabolizing enzyme)

activity leads to accumulation of intracellular cyclic AMP. The specific mechanism by which roflumilast exerts its therapeutic action is not well defined.

Recommendation: Zorvye® to non-preferred.

Ztalmy® (ganaxolone suspension); **PDL category**- Anticonvulsants

Ganaxolone, the active ingredient of Ztalmy®, is a neuroactive steroid gamma-aminobutyric acid A (GABA-A) receptor positive modulator. The exact mechanism of action by which ganaxolone exerts its therapeutic effects for its approved indication is not known, but its anticonvulsant effects are thought to result from positive allosteric modulation of the GABA-A receptor in the CNS. It is indicated for the treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) in patients 2 years of age and older. The safety and efficacy of Ztalmy® for the treatment of seizures associated with CDD were assessed in a single, double-blind, randomized, placebo-controlled study that included patients 2 to 19 years of age. The primary efficacy endpoint was the percentage change in the 28-day frequency of major motor seizures, and patients receiving Ztalmy® had a significantly greater reduction in the 28-day frequency of major motor seizures as compared to patients receiving placebo. There is no evidence at this time to support that Ztalmy® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Ztalmy® to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

None at this time

Board Decision: No action.

ADJOURNMENT: 8:30PM

The next meeting will be held on **March 14, 2023** 530pm-8pm hybrid.